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Becker Nevus Syndrome

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The new term Becker nevus syndrome is proposed for a phenotype characterized by the presence of a particular type of organoid epithelial nevus showing hyperpigmentation, increased hairiness and hamartomatous augmentation of smooth muscle fibers, and other developmental defects such as ipsilateral hypoplasia of breast and skeletal anomalies including scoliosis, spina bifida occulta, or ipsilateral hypoplasia of a limb. The present review includes 23 cases that can be categorized under this designation. The Becker nevus syndrome usually occurs sporadically. The associated anomalies tend to show a definite regional correspondence, suggesting a common origin from an early postzygotic mutation. Am. J. Med. Genet. 68:357–361, 1997. **© 1997 Wiley-Liss, Inc.**

KEY WORDS: pigmented hairy epidermal nevus; cutaneous smooth muscle hamartoma; unilateral hypoplasia of breast; skeletal defects; scoliosis; hemivertebrae; spina bifida occulta; fused ribs; asymmetrical shortening of limbs

INTRODUCTION

The Becker nevus is a rather common skin lesion characterized by circumscribed hyperpigmentation with an irregular outline and hypertrichosis [Tymen et al., 1981] (Fig. 1). This mostly unilateral cutaneous anomaly was first delineated by Becker [1949]. Following the rules regarding eponymic designations as recommended by McKusick [1994] we prefer to avoid the possessive form "Becker's nevus," because the eponym merely serves as a "handle." This skin lesion does not belong to the group of melanocytic nevi but represents a specific form of organoid epithelial nevus [Frain-Bell and Rook, 1957; Haneke, 1979].

In the past, several authors have reported cases of Becker nevus associated with other anomalies such as unilateral hypoplasia of breast or scoliosis [Mascaró et al., 1970; Glinick et al., 1983; Moore and Schosser, 1985]. However, this association has so far not received much attention. In particular, no specific name was given to this phenotype until 1995 when the term "pigmented hairy epidermal nevus syndrome" was proposed by one of us [Happle, 1995]. Here, a definition of this syndrome is presented, the spectrum of associated anomalies known so far is reviewed, and the new designation "Becker nevus syndrome" is proposed.

Definition of the Syndrome

Becker nevus syndrome is a phenotype characterized by the presence of a Becker nevus in association with unilateral hypoplasia of breast or other cutaneous, muscular or skeletal defects. Usually, but not invariably, all of these anomalies involve the same side of the body.

Clinical Spectrum of the Syndrome

An overview of the anomalies occurring in Becker nevus syndrome is presented in Table I.

Becker Nevus

This cutaneous anomaly, which is also known under the term pigmented hairy epidermal nevus [Copeman and Jones, 1965], constitutes a hallmark of the Becker nevus syndrome, although it mostly occurs as an isolated skin disorder. Typically, the lesion has bizarre outlines reminiscent of an archipelago. It often involves the thorax but has also been observed in many other regions of the body [Siemens, 1967]. A systematized involvement that may be either unilateral or bilateral has likewise been described [Panizzon et al., 1984]. During adolescence, the Becker nevus may be superimposed by acne-like lesions [Burgreen and Ackerman, 1978; Bardach, 1979]. Histopathological examination shows that the epidermal component of this anomaly is characterized by slight acanthosis and hyperpigmentation of basal cells. The dermal component consists of numerous bundles of smooth muscle fibers unrelated to hair follicles ("smooth muscle hamartoma") [Haneke, 1979]. For an appropriate classification of this nevus, it is important to realize that no nevomelanocytic structures are found in the lesion.

Because this is an androgen-dependent anomaly [Person and Longcope, 1984], the "full-blown" picture of Becker nevus is in general observed exclusively in adolescent or adult men. In women and prepubertal boys the lesion is much less conspicuous because the pig-

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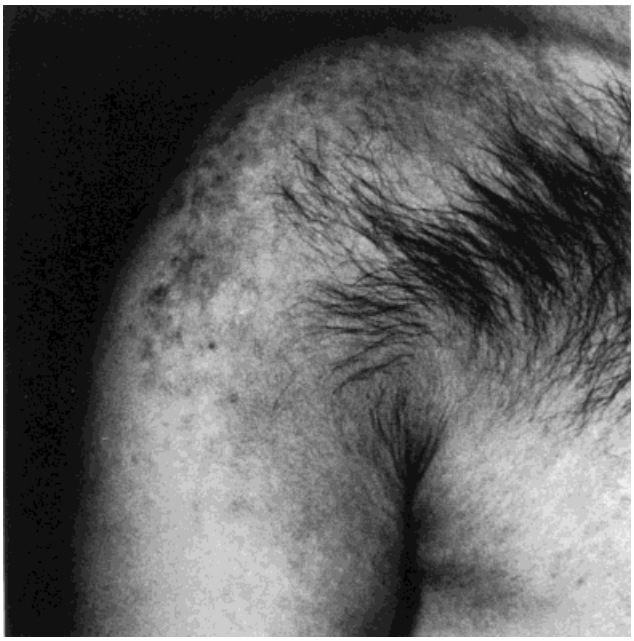

Fig. 1. Becker nevus characterized by circumscribed hyperpigmentation with an irregular outline reminiscent of an archipelago in an adult man. Increased hairiness is particularly marked in men.

mentation is less intense and hairiness is absent or only mild. This explains a skewed sex ratio of isolated Becker nevus as reported in the literature, with a fourfold preponderance of men [Panizzon et al., 1984; Hulsmans et al., 1989]. It seems reasonable to assume that the true sex ratio is 1:1 [Happle 1995].

Unilateral Hypoplasia of Breast

Women affected with Becker nevus often show an ipsilateral hypoplasia of breast [Naranjo et al., 1971; Friedel et al., 1988; van Gerwen et al., 1993; Cambiaghi et al., 1994] (Fig. 2). This developmental defect was documented in 11 of 16 women included in the present review (Table I). It involves the fatty tissue as well as the nipple and the areola [Glinick et al., 1983].

Unilateral Hypoplasia of the Shoulder Girdle

Lambert et al. [1994] observed ipsilateral hypoplasia of the shoulder girdle. Ipsilateral absence of the pectoralis major muscle was documented by Moore and Schosser [1985].

Hypoplasia of the Ipsilateral Arm

Shortness of the ipsilateral arm was reported by Copeman and Jones [1965], Moore and Schosser [1985], Glinick et al. [1983], as well as by Glinick and Alper [1986]. Asymmetry of limbs was also noted by Lucky et al. [1981] and Blanc et al. [1988]. They described this as an enlargement of the ipsilateral limb but it cannot be excluded that in fact the asymmetry was caused by hypoplasia of the contralateral limb.

Vertebral Defects and Scoliosis

X-ray films of the vertebral column may demonstrate hemivertebrae or spina bifida occulta [Naranjo et al., 1980; Glinick et al., 1983]. Scoliosis is clearly associated with this syndrome [Mascaró et al., 1970; Smolle, 1983; Formigón et al., 1992]. Hulsmans et al. [1989] examined a group of 40 patients affected with Becker nevus and found scoliosis in 28.2% of cases, a prevalence 10 times higher than observed in the general population (3%).

Other Skeletal Anomalies

Additional skeletal anomalies observed in association with Becker nevus include fused or accessory cervical ribs [Hulsmans et al., 1989], pectus excavatum [Glinick and Alper, 1986], pectus carinatum [Glinick et al., 1983], and bilateral internal tibial torsion [Moore and Schosser, 1985].

Other Cutaneous Anomalies

Extensive patchy hypoplasia of ipsilateral subcutaneous fatty tissue has been observed by van Gerwen et al. [1993]. In addition, hypoplasia of the contralateral labium minus was noted in this case. Szylit et al. [1986] described an accessory scrotum. Other reports have documented sparse hair of the ipsilateral axilla [Glinick et al., 1983], a circular depressed area within the ipsilateral temporal region [Glinick et al., 1983], and an umbilical hernia [Moore and Schosser, 1985].

DISCUSSION

From this review, the Becker nevus syndrome emerges as a distinct entity. The most characteristic manifestations are Becker nevus, ipsilateral hypoplasia of breast and ipsilateral skeletal defects, but contralateral anomalies may also be present. To give this syndrome a name may help to delineate further the spectrum of associated defects.

The Becker nevus syndrome can be categorized as a particular type of epidermal nevus syndrome. By its characteristic clinical appearance it can be easily distinguished from other epidermal nevus syndromes such as Schimmelpenning syndrome, Proteus syndrome or CHILD syndrome [Happle, 1995]. Contrasting with these phenotypes, the Becker nevus syndrome has so far no entry in McKusick's catalog of human genes and genetic disorders [McKusick, 1994].

The Becker nevus syndrome should not be confused with "Becker syndrome," an eponymic term proposed by Bleehen et al. [1992] for a phenotype characterized by discrete or confluent brown macules on the neck and forearms, as observed by Becker and Reuter [1939] in several members of a family.

The male to female ratio of cases of Becker nevus syndrome so far reported is approximately 1:2 (Table I). This can be best explained by the fact that, as an easily recognizable anomaly, cases of unilateral hypoplasia of breast have rather often been reported, reversing the sex ratio as compared to isolated Becker nevus. More thorough clinical studies will probably show that the true sex ratio is approximately 1:1.

TABLE I. Spectrum of Anomalies Reported in Association With Becker Nevus

Reference	Age (yrs)	Sex	Localization of Becker nevus	Unilateral hypoplasia of breast	Skeletal anomalies	Other anomalies
Copeman and Jones [1965]						
Case 1	23	F	R chest	R		
Case 6	26	F	L arm		Short L arm	
Mascaró et al. [1970]						
Case 7	22	M	L abdomen		Herniated disc T10	
Case 18	22	F	L chest	L	Thoracic scoliosis	
Naranjo et al. [1980]	20	M	R chest		Spina bifida L5	
Lucky et al. [1981]	12	F	R leg		Asymmetry of feet (R > L)	
Glinick et al. [1983]						
Case 1	25	F	L chest and arm	L	Short L arm, spina bifida occulta	Circular depressed area in the L temporal region
Case 2	12	M	L chest and abdomen		Pectus carinatum, spina bifida occulta L5	
Smolle [1983]	23	F	L shoulder		Scoliosis	
Moore and Schosser [1985]	14	F	R shoulder and arm	R	Bilateral internal tibial torsion	Absence of R pectoralis major muscle; umbilical hernia
Glinick and Alper [1986]						
Case 1	?	M	Chest		Pectus excavatum	
Case 2	?	F	Chest		Pectus excavatum	
Case 3	?	M	Arm		Hypoplasia of ipsilateral arm	
Szylit et al. [1986]	36	M	L buttock			Accessory scrotum
Friedel et al. [1988]	17	F	R breast L groin	R		Supernumerary nipple (L)
Blanc et al. [1988]	17	F	R breast and axilla	R	Asymmetry of arms (R > L)	
Hulsmans et al. [1989]	2	M	Shoulder		Scoliosis with ipsilateral vertebral defects (hemivertebrae); accessory cervical rib; fused ribs	
Formigón et al. [1992]						
Case 1	16	F	R trunk	R	Lumbar scoliosis	
Case 2	14	F	L chest	L	Lumbar scoliosis	
van Gerwen et al. [1993]	50	F	L trunk, both thighs	L		Unilateral hypoplasia of subcutaneous tissue of trunk (L); hypoplasia of labium minus (R)
Cambiaghi et al. [1994]	33	F	R chest and arm	R		
Lambert et al. [1994]	20	F	L shoulder			Ipsilateral hypoplasia of shoulder girdle; congenital adrenal hyperplasia; chromosomal mosaicism (small accessory chromosome in 8% of fibroblasts from Becker nevus (vs 1% from contralateral area))
Smolle [1994][a]	17	F	L breast	L		

[a]Personal communication.

Fig. 2. Becker nevus showing unilateral arrangement on the abdomen and ipsilateral hypoplasia of breast in a 50-year-old woman. Asymmetry has been partly corrected by a reduction mammoplasty on the right and a silicon prosthetic implant in the left breast, as well as by a lipectomy on the right side of the abdomen (for a detailed report of this case see van Gerwen et al. [1993]).

Although scoliosis certainly belongs to the spectrum of this phenotype [Hulsmans et al., 1989], it seems important from a heuristic point of view to realize that in a given case a co-occurrence of Becker nevus and very mild scoliosis is not sufficient to firmly establish a diagnosis of Becker nevus syndrome.

This overview documents a remarkable regional correspondence between the Becker nevus and associated anomalies, suggesting a common origin from an early postzygotic mutational event giving rise to mosaicism. For example, the frequently occurring hypoplasia of breast was always ipsilateral and the associated Becker nevus involved the thorax. The skeletal defects observed in this syndrome likewise tended to involve regions corresponding to the area of Becker nevus. An accessory scrotum was found in combination with a Becker nevus covering the gluteal region [Szylit et al., 1986].

All of the cases of Becker nevus syndrome reported so far have been sporadic. Lambert et al. [1994] described mosaicism involving a small extra chromosome predominantly present in fibroblasts derived from the area of Becker nevus. The genetic basis of this syndrome is not clear but it has been proposed that the phenotype results from loss of heterozygosity for the underlying allele [Happle, 1995]. Interestingly, Wagner et al. [1989] have observed a case of Becker nevus arranged in close proximity to unilateral nevoid teleangiectasia. This association has been taken as a possible example of twin spotting, implying allelic loss by somatic recombination [Happle, 1993]. This mechanism would explain why an isolated Becker nevus usually occurs as a sporadic lesion but exceptionally may show familial aggregation [Gartmann et al., 1968; Fretzin and Whitney, 1985; Panizzon and Schnyder, 1988; Jain and Fisher, 1989]. In the future, the Becker nevus syndrome will presumably likewise be shown to affect, by way of exception, several members of a family. Heterozygous individuals would be, as a rule, phenotypically normal, and the responsible allele would therefore be transmitted unperceived through many generations. The nevus and the associated anomalies would only develop when a somatic recombination occurs at an early stage of embryogenesis, resulting in a mosaic population of homozygous cells. Because this phenotype would be neither simply mendelian nor entirely nonmendelian, the new term "paradominant inheritance" has been proposed [Happle, 1992]. Future clinical and molecular research should show whether this concept holds true.

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